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EXAMINER
ZITOMER, STEPHANIE W

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 08/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/926,201	GONZALEZ ET AL.	
	Examiner	Art Unit	
	Stephanie Zitomer	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 December 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Search exchange pilot program

1. The USPTO is participating in a search exchange pilot program with the European Patent Office (EPO). As part of the pilot program, the USPTO has received a copy of the Search Report prepared by the EPO on the counterpart EP application for which priority under 35 U.S.C. 119(a) is claimed. The references listed in the EPO Search Report have been listed in the 1449 form accompanying the Information Disclosure Statement submitted by applicant. The 1449 has been initialed and signed by the examiner and is attached to this Office action.

Priority benefit

2. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)).

Objection to the disclosure: Informalities

3. The disclosure is objected to because of the following informalities:

(a) Nucleotide and amino acid sequences appearing in the disclosure must have SEQ ID NOS: (37 CFR 1.821). Sequences lacking SEQ ID NOS: are found at page 11, line 23; page 15, lines 16, 25, 32; page 16, lines 1, 15; page 17, lines 26-29.

(b) "Epicurean" has been substituted for *Escherichia*, the genus name of *E. coli* at page 12, line 24 and page 16, line 9.

Appropriate correction is required.

Rejection under 35 U.S.C. 112, second paragraph: Indefiniteness

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-11 and 16-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) In claim 1 (e), "the nucleic acid insert' lacks antecedent basis in the prior steps. It is suggested to change "contained" in step (a) to

--inserted-- to provide antecedent basis.

(b) Claims 1 and 2 are confusing in "library of random nucleic acids" which has more than a single meaning and is not defined in the claims or in the specification. Random nucleic acids may mean having a random nucleotide sequence or randomly cleaved as by shearing or even randomly cleaved with restriction endonucleases when the presence of their binding sites in the nucleic acid is not known. Thus, one of ordinary skill in the art would not be reasonably apprised of the scope of the claimed invention. It is suggested to clarify the claims by indicating which definition applies and as only that of cleavage with restriction enzymes is supported by the specification, it appears to be the most appropriate.

(c) Claim 2 is confusing in reciting "eukaryotic or yeast library is used" because yeast are eukyarotes.

(d) Claim 9 is confusing because "marker gene" lacks antecedent basis in claim 1 which recites "reporter gene". It is suggested to changer "marker" to --reporter--.

(e) Claim 10 is confusing because the recitation "the nucleic acid is used to detect DNA sequences..." at lines 5-7, is *non sequitur* to the preamble because it is directed to a DNA assay for identification of a nucleic acid whereas the preamble states the method is "for identification and/or production of a protein...". For the same reason, claim 11 lacks antecedent basis in claim 10. It is suggested to clarify claims 10 and 11 as nucleic acid assays or protein production methods.

(f) Claim 15 lacks antecedent basis in claim 12 for "reporter gene product" which is not recited in the latter claim. It is suggested to change the claim 15 dependency to claim 13 which does recite the reporter gene.

(g) Claims 16-22 are confusing because "desired protein" in the last line lacks antecedent basis elsewhere in the claim.

Rejections under 35 U.S.C. 102(b): Anticipation

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1, 3, 4 and 7-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Sawin et al. (PNAS *USA* 94:15146-15151, December 24, 1996). Sawin et al. disclose the method of claim 1 for detection, cloning and/or sequencing of polypeptides or parts thereof which drive the subcellular localization of a protein containing such polypeptide or part thereof (page 15146, Abstract) comprising (a) constructing an expression library of random nucleic acids ligated to a reporter gene and contained in a vector (page 15146, paragraph 3); (b) transfecting a plurality of host cells with the library (page 15146, paragraph 4); (c) screening for subcellular localization of the expression product of the nucleic acid via detection of a signal produced by the reporter gene expression product (page 15146, paragraph 4 and bridging page 15147); (d) cloning cells in which the reporter gene expression product signal is detected in a certain subcellular localization (page 15147, full paragraphs 2 and 3); and (e) cloning and optionally sequencing the nucleic acid insert which encodes the polypeptide or part thereof (page 15147, full paragraphs 2-4).

Regarding claims 3 and 4, Sawin et al. disclose the claim 1 embodiments wherein a yeast library and a homologous system, i.e., yeast nucleic acid in yeast cells, is used (page 15146, paragraphs 2 and 3).

Regarding claims 7 and 8, Sawin et al. disclose the claim 1 embodiments wherein a reporter gene leading to a visually detectable signal upon expression is used and the reporter gene is nucleic acid encoding GFP (page 15146, paragraphs 2-4).

Regarding claim 9, Sawin et al. disclose the claim 1 embodiment wherein the vector contains an inducible promoter driving expression of random nucleic acids and reporter gene (page 15147, Figure 1 and text below it at line 5).

Regarding claims 10 and 11, Sawin et al. disclose the embodiments wherein the nucleic acid coding for a polypeptide or part thereof driving the localization in the subcellular location is cloned and used in an expression system for production of the protein (page 15147, full paragraphs 2-4).

6. Claims 16-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Gordon-Kamm et al. (WO 97/41228). Regarding claims 16 and 17, the claimed expression vector comprising a DNA sequence encoding a polypeptide or part thereof which drives the subcellular localization of a protein containing the polypeptide or part thereof fused to a DNA sequence encoding a desired protein (claim 16) wherein the vector is a eukaryotic vector (claim 17) is disclosed by Gordon-Kamm et al. (page 76, Example 6, lines 5-17). The embodiments of claims 18 and 19 wherein the vector further comprises a reporter gene positioned in such a way that a fusion protein of desired protein and polypeptide or part thereof and reporter product are encoded (claim 18) and the reporter gene product is visually detectable (claim 19) are also disclosed (page 76, lines 5-17

Rejection under 35 U.S.C. 102(e): Anticipation

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an

application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 1, 5, 7-14, 16-19, 21 and 23 are rejected under 35 U.S.C. 102(e) as being anticipated by Anderson et al. (6,180,343 filed October 8, 1998). Anderson et al. disclose the method of claim 1 for detection, cloning and/or sequencing of polypeptides or parts thereof which drive the subcellular localization of a protein containing such polypeptide or part thereof comprising (a) constructing an expression library of random nucleic acids ligated to a reporter gene and contained in a vector (column 4, lines 63-67; column 5, lines 6-8; column 18, lines 30-32); (b) transfecting a plurality of host cells with the library (column 19, lines 55-59); (c) screening for subcellular localization of the expression product of the nucleic acid via detection of a signal produced by the reporter gene expression product (column 23, lines 16-24, 41-42); (d) cloning cells in which the reporter gene expression product signal is detected in a certain subcellular localization; and (e) cloning and optionally sequencing the nucleic acid insert which encodes the polypeptide or part thereof (column 25, lines 16-36).

Regarding claim 5, the claim 1 embodiment wherein a heterologous system of library and cells is used is disclosed by Anderson et al. (column 20, lines 45-47).

Regarding claims 7 and 8, the claim 1 embodiment wherein a reporter gene leading to a visually detecable signal upon expression is used and nucleic acids coding for GFP are used as the reporter gene, respectively, are disclosed by Anderson et al. (Abstract, lines 1-3).

Regarding claim 9, the claim 1 embodiment wherein the vector contains an inducible promoter is disclosed by Anderson et al. (column 19, lines 8-9).

Regarding claims 10 and 11, the embodiment wherein for the production of the protein the nucleic acid is expressed in an expression system is disclosed by Anderson et al. (column 19, lines 55-59).

Regarding claim 12, the embodiment wherein a nucleic acid encoding a polypeptide or part thereof driving subcellular localization obtained by the method of claim 1 is fused to a nucleic acid

encoding a protein to be expressed and the fusion product is expressed is implicit in Anderson et al. because the reference discloses obtaining such a nucleic acid sequence encoding a target or signaling sequence polypeptide that localizes in a subcellular location by a method identical to that of claim 1 (column 23, lines 16-28, 41-42) and the reference further discloses using a polypeptide or part thereof as a targeting sequence (column 7, line-59-column 8, line 1; column 11, 22-36) or a signal sequence (column 11, lines 29-31) and the fusion product is expressed (column 25, lines 16-30).

Regarding claim 13, the claim 12 embodiment wherein a nucleic acid coding for the polypeptide or part thereof and a reporter gene are fused to the nucleic acid coding for a protein to be expressed is disclosed by Anderson et al. (column 15, lines 38-49).

Regarding claim 14, the embodiment of claim 12 wherein the expression product of the reporter gene is visually detectable is disclosed by Anderson et al. (column 15, lines 48-49).

Regarding claim 16, Anderson et al. disclose the claimed vector comprising a DNA sequence encoding a fusion protein comprising a polypeptide or part thereof which drives the subcellular localization of a protein containing such polypeptide or part thereof and a desired protein (column 7, line 56-column 8, line 1; column 11, line 22-37, esp. lines 30-34; column 18, lines 30-33).

Regarding claim 17, the claim 16 embodiment wherein the vector is a eukaryotic vector is disclosed by Anderson et al. (column 19, lines 12-16).

Regarding claims 18 and 19, the claim 16 and 17 embodiments wherein the vector further comprises a reporter gene such that a reporter fused to the fusion protein is encoded and the reporter gene product is visually detectable are disclosed by Anderson et al. (column 17, lines 8-11; column 18, lines 30-33).

Regarding claims 21 and 23, Anderson et al. disclose the claim 16 embodiment compising a cell line and collection thereof transfected with a vector of claim 16 (column 20, lines 10-11; column 28, lines 16-17).

Rejection under 35 U.S.C. 103(a): Obviousness

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sawin et al. (paragraph 5 above) as applied to claim 1 above, and further in view of Stewart et al. (20001/002254 A1). Regarding claim 2, the embodiment of the claim 1 method wherein "a cDNA or cDNA fragments are used as random nucleic acids" differs from the method of Sawin et al. in the use of cDNA. However, it was routinely practiced in the art to make random cDNA or cDNA fragment libraries for gene and polypeptide screening as taught by Stewart et al. (page 4, paragraphs 0036, 0044). It would have been obvious to the skilled practitioner in the art at the time the claimed invention was made to use cDNA and cDNA fragment libraries in the method disclosed by Sawin et al. because one of ordinary skill in the art would have been motivated to employ random fragments of cDNA instead of genomic DNA for the benefit of having a higher expectation of identifying polypeptides that exhibit subcellular localization in view of the Sawin et al. interest in such polypeptides as shown by their characterization of one such polypeptide, S26,

which appeared to be a protein associated with heterochromatin (page 15151, penultimate paragraph). It would have been known in the art that the higher expectation would have derived from the absence from cDNA of sequences extraneous in the method context such as introns, regulatory sequences and repetitive sequence regions occurring in genomic DNA.

9. Claims 5 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sawin et al. (paragraph 5 above) as applied to claim 1 above, and further in view of Stewart et al. (20001/002254 A1). The claim 1 method embodiments of claims 5 and 6 differ from the Sawin et al. method which is identical to that of claim 1 wherein in a heterologous system of library and host cells (claim 5) a *Drosphila* library and mammalian or yeast cells are used (claim 6). However, a heterologous system according to Sawin et al. would have been obvious to one of ordinary skill in the art at the time the claimed invention was made because the skilled practitioner in the art would have been motivated to select the library source and host cells according to experimental design parameters, desired results and available materials for the benefit of of identifying subcellular localising polypeptides of other organisms. In particular, the skilled practitioner in the art would have been motivated to employ a *Drosophila* library in the yeast cells of Sawin et al. in view of the historical relationship of *Drosophila* proteins and pathways with those of higher organisms as taught by Stewart et al. (page 1, paragraph 0004) and the further teaching of cloning in mammalian and yeast cells (page 6, paragraph 0060) and a *Drosophila* library (page 5, paragraph 0054).

10. Claims 15 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al. (paragraph 6 above) as applied to claims 1, 12 and 16 above, and further in view of Cha et al. (Biotechnol. Prog. 15(2):283-286, 1999). The fused nucleic acid embodiments of claims 15 and 20 differ from that of Anderson et al. wherein a proteolytic cleavage site is inserted between one or more of the component polypeptide sequences. However, Cha et al. teach a general purpose nucleic acid construct comprising a reporter gene, proteolytic cleavage site and gene of interest (page 283, Figure 1 and fourth paragraph). It would have been obvious and the skilled practitioner

in the art would have been motivated at the time the claimed invention was made to employ a proteolytic cleavage site in the fused nucleic acids of Anderson et al. (e.g., column 18, lines 30-43) for the benefit of isolating the polypeptide of interest as taught by Cha et al. (page 283, fourth paragraph) and for the obvious benefit of enabling reuse of the reporter gene in another such construct.

11. Claims 22 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al. (paragraph 6 above) as applied to claims 16 and 21 above, and further in view of Ahern (http://www.the-scientist.library.upenn.edu/yr1995/july/tools_950724.html). The vector and cell line embodiments of claims 22 and 24 differ from those of Anderson et al. wherein the vector and cell line, respectively, are each contained in a kit. However, the packaging of reagents for particular applications was routinely practiced in the art as taught by Ahern (page 4, paragraphs 5 and 6). Accordingly, it would have been obvious and one of ordinary skill in the art would have been motivated at the time the claimed invention was made to package the vectors and cell lines of Anderson et al. for the obvious benefits of convenience, time saving and commercial applications a taught by Ahern (page 4, paragraph 2).

Conclusion

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephanie Zitomer whose telephone number is (703) 308-3985. The examiner can normally be reached on Monday through Friday from 10:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152. The official fax phone number for this Group is (703) 308-4242. The unofficial fax number is (703) 308-8724. The examiner's Rightfax number is 703-746-3148.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196. For questions and requests relating to formal matters contact LIE Chantae Dessau at 703-605-1237.

Stephanie Zitomer, Ph.D.
August 25, 2003

STEPHANIE W. ZITOMER
PRIMARY EXAMINER